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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,340	09/25/2003	Denis Gravel	GOUD:038US	4251

7590 01/14/2005

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 01/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/671,340	GRAVEL ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19*

is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040521;20040802*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Sequence Listing filed September 25, 2003 has been approved.

2. The disclosure is objected to because of the following informalities: Paragraph [0013] of the specification recites that an Ala-Asp bond in human GLP-1 is enzymatically cleaved in the circulation. However, there is no Ala-Asp bond in the amino acid sequence recited in the paragraph. Appropriate correction is required.

3. Claims 1, 2, and 4-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, section i, recites a C_1 alkenoic acid, and claim 1, section ii, recites a C_1 alkynoic acid. However, it is not possible to have a double or triple bond involving just a single carbon atom. In both sections, it is believed that "C_1" should be changed to "C_2". In claim 2, the variable "R" is not defined in the claim.

4. Claims 1-19 are objected to because of the following informalities: At claim 1, line 4, "val" should be changed to "Val". Appropriate correction is required.

5. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Not all of the X groups recited in claim 2 are embraced by the definition of X recited in independent claim 1. With respect to the first and third groups of claim 2, these arylalkanoic acids are not substituted as required by independent claim 1, section iv. With respect to the ninth group of claim 2, the NH(phenyl) substituent is not permitted by independent claim 1, section iv. With respect to the tenth group of claim 2, the phenyl-S-substituent is not permitted by independent claim 1, section i.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-9 and 17-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 103 and 112-115 of copending Application No. 10/343,654. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '654 application anticipate instant claims 1-3. With respect to instant claims 4 and 19, while the '654 application does not claim combining its modified GLP-1 with a pharmaceutically acceptable carrier, diluent, or excipient, it would have been obvious to one of ordinary skill in the art to combine the claimed modified GLP-1 of the '654 application with pharmaceutically acceptable carriers, diluents, and excipients, because the claimed modified GLP-1 of the '654 application is intended to be used pharmaceutically, and it is routine in the pharmaceutical arts to combine active agents with pharmaceutically acceptable carriers, diluents, and excipients for ease of storage, transport, measurement, and administration. With respect to instant claim 5, it would have been obvious to one of ordinary skill in the art to determine all operable and optimal amounts for the claimed modified GLP-1 of the '654 application because amount is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts. With respect to

instant claims 6-9, while the '654 application does not claim a method of treating diseases or conditions with the claimed GLP-1 analogs it would have been obvious to one of ordinary skill in the art to administer the claimed modified GLP-1 of the '654 application consistent with its claimed intended uses. With respect to instant claim 17, while the '654 application does not claim any particular administration route for its claimed modified GLP-1, it would have been obvious to one of ordinary skill in the art to administer the claimed modified GLP-1 of the '654 application subcutaneously, intravenously, transdermally, orally, buccally, or intranasally because these are common pharmaceutical methods for administering peptides including GLP-1. With respect to instant claim 18, while the '654 application does not claim administering its claimed modified GLP-1 to humans, it would have been obvious to one of ordinary skill in the art to administer the claimed modified GLP-1 of the '654 application to humans because the claimed GLP-1 of the '654 application is intended to be used to treat insulin resistance and Type II diabetes, and humans are known to suffer from these disorders.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 10-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 103 and 112-115 of copending Application No. 10/343,654 in view of the WO Patent Application 98/08871, the Drucker article (Endocrinology, Vol. 142, pages 521-527), the WO Patent Application 99/43707, or the Toft-Nielsen et al article (Diabetes Care, Vol. 22, pages 1137-1143). The '654 application does not claim administering its modified GLP-1 for the purposes recited in the instant claims. The WO Patent Application '871 teaches the use of GLP-1 to treat Types I and II diabetes and

obesity (see, e.g., page 5, lines 3-4, page 30, lines 24-26). The Drucker article teaches that GLP-1 increases pancreatic beta cell mass, lowers appetite, and stimulates insulin secretion (see page 523, column 2, first full paragraph, and the paragraph bridging pages 523 and 524). The WO Patent Application '707 teaches administering GLP-1 to treat diabetes, obesity, and insulin resistance (see, e.g., page 25, lines 14-30). The Toft-Nielsen et al article discloses administering GLP-1 to human patients with Type 2 diabetes, whereby fasting plasma glucose is decreased, plasma insulin levels are increased, and satiety is increased (see, e.g., the Abstract). It would have been obvious to one of ordinary skill in the art to administer the claimed modified GLP-1 of the '654 application for the purposes claimed by Applicants, because the claimed purposes are known uses of GLP-1 as shown by the secondary references discussed above, and because the '654 application intends to use its claimed modified GLP-1 for the same purposes that unmodified GLP-1 is used.

This is a provisional obviousness-type double patenting rejection.

9. Claims 1-19 are directed to an invention not patentably distinct from claims 103 and 112-115 of commonly assigned 10/343,654. Specifically, see the above provisional obviousness-type double patenting rejections.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/343,654, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the

assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

10. Instant claims 2 and 3 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/413,171 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed invention.

Instant claims 1 and 4-19 are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/413,171 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, does not disclose X as defined in claim 1, sections iv and v, in which the alkanoic portion of the arylalkanoic or heteroarylalkanoic acid can be substituted by lower alkyl, lower alkoxy, lower alkylthio, halo, hydroxy, trifluoromethyl, amino, -NH(lower alkyl), -N(lower alkyl)$_2$, di- and tri-substituted phenyl, 1-naphthyl, and 2-naphthyl (note that in the provisional application, it is the aryl group in particular, and not the arylalkanoic or heteroarylalkanoic acid in general, which is substituted); does not disclose X as defined in claim 1, sections iv and v, in which the 1-naphthyl and 2-naphthyl groups are substituted with methyl, methoxy, methylthio, halo, hydroxy, or amino (in the provisional application, only the di- and tri-substituted phenyl is substituted with these substituents); does not disclose treating or preventing diseases or conditions associated with a

disorder of glucose metabolism in general; does not disclose treating or preventing weight disorders or associated conditions in general; and does not disclose reducing blood glucose levels in general (i.e., including non-fasting blood glucose levels). The corresponding disclosures in the provisional application are narrower in scope than what is claimed in the instant application, and disclosure of a species or subgenus does not provide written descriptive support for purposes of priority claims. See MPEP 201.11(VI).

Accordingly, because the WO Patent Application 02/10195 has a different inventorship than the instant application, the WO Patent Application '195 is available as prior art against instant claims 2 and 3 under 35 U.S.C. 102(a) and (e), and is available as prior art against instant claims 1 and 4-19 under 35 U.S.C. 102(b).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

12. Claims 1, 4-6, 17, and 19 are rejected under 35 U.S.C. 102(b) and claims 2 and 3 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by the WO Patent Application 02/10195. The WO Patent Application '195 teaches GLP-1 modified at its N-terminus with compounds 2, 13, 60, and 63. The modified GLP-1 is combined with vehicle and administered subcutaneously to mice in amounts of 1, 5, and 10 mcg, and decreases blood glucose levels after an oral glucose challenge. See Example 1.

13. Claims 7-16 and 18 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 02/10195 as applied against claims 1-6, 17, and 19 above, and further in view of the WO Patent Application 98/08871, the Drucker article (Endocrinology, Vol. 142, pages 521-527), the WO Patent Application 99/43707, or the Toft-Nielsen et al article (Diabetes Care, Vol. 22, pages 1137-1143). The WO Patent Application '195 does not teach administering its

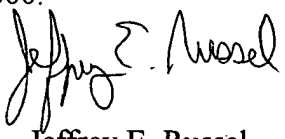
modified GLP-1 for the purposes recited in the instant claims. The WO Patent Application '871 teaches the use of GLP-1 to treat Types I and II diabetes and obesity (see, e.g., page 5, lines 3-4, page 30, lines 24-26). The Drucker article teaches that GLP-1 increases pancreatic beta cell mass, lowers appetite, and stimulates insulin secretion (see page 523, column 2, first full paragraph, and the paragraph bridging pages 523 and 524). The WO Patent Application '707 teaches administering GLP-1 to treat diabetes, obesity, and insulin resistance (see, e.g., page 25, lines 14-30). The Toft-Nielsen et al article discloses administering GLP-1 to human patients with Type 2 diabetes, whereby fasting plasma glucose is decreased, plasma insulin levels are increased, and satiety is increased (see, e.g., the Abstract). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the modified GLP-1 of the WO Patent Application '195 for the purposes claimed by Applicants, because the claimed purposes are known uses of GLP-1 as shown by the secondary references discussed above, and because the WO Patent Application '195 intends to use its modified GLP-1 for the same purposes that unmodified GLP-1 is used.

14. Dong (U.S. Patent Application Publication 2004/0018981) is cited as art of interest, but is not deemed to teach or suggest the instant claimed compounds. Note firstly that Dong does not permit the GLP-1 being modified to have the same amino acid sequence as Applicants' SEQ ID NO:1. See, e.g., claim 1, proviso (i) of Dong et al. Note also that in claim 1 of Dong, where one of R^2 and R^3 can be $C(O)X^5$ and X^5 can be $(C_2\text{-}C_{30})$alkenyl, phenyl$(C_1\text{-}C_{30})$alkyl, naphthyl $(C_1\text{-}C_{30})$alkyl, or hydroxy$(C_2\text{-}C_{30})$alkenyl, these groups are not substituted as required by instant claim 1, sections i and iv. In claim 1 of Dong where one of R^2 and R^3 can be one of the two heterocyclic structures and r=0 and Y is H, or where one of R^2 and R^3 can be hydroxyphenyl$(C_1\text{-}$

C_{30})alkyl or hydroxynaphthyl (C_1-C_{30})alkyl, the substituents do have structures which satisfy the requirements of instant claim 1, section iv. However, these particular substituents of Dong are not preferred substituents (see, e.g., section [0070]), and as noted above, Dong in and of itself does not teach or suggest their use in modifying GLP-1(7-36). In the absence of any discussion of the functions and/or biological effects of the R^2 and R^3 substituents of Dong, there is not deemed to be motivation to chose the particular R^2 and R^3 substituents of Dong discussed above and to use them to modify GLP-1(7-36).

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

January 11, 2005